# PRO 2000

**Drug Class:** **Microbicides**

## Drug Description

PRO 2000 is a naphthalene sulfonic acid polymer. The polymer is polyanionic and consists of alternating 2-naphthalene sulfonic acid sodium salt and methylene units. [1]

## HIV/AIDS-Related Uses

PRO 2000 is an antimicrobial intravaginal gel being investigated for the prevention of HIV and other sexually transmitted diseases.[2]

## Non-HIV/AIDS-Related Uses

In laboratory tests and in animal studies, PRO 2000 demonstrated activity against Chlamydia trachomatis, Neisseriae gonorrheae, and herpes simplex virus.[3]

## Pharmacology

Mechanistically, PRO 2000 disrupts the initial binding and membrane fusion steps of HIV-1 infection.[4] PRO 2000 binds to CD4 with nanomolar affinity and blocks CD4 binding to HIV gp120. It inhibits infection by a wide range of HIV isolates in a variety of cell types.[5]

Following topical administration of naphthalene 2-sulfonate polymer in animals and intravaginal application in humans, no systemic absorption was detected.[6] PRO 2000 was undetectable in plasma samples collected from three separate Phase I studies, suggesting that negligible systemic absorption of PRO 2000 occurs following intravaginal administration.[7] [8]

PRO 2000 is completely compatible with the use of latex condoms. This may offer women an appealing alternative or complement to condoms, providing women with a means to control disease transmission. PRO 2000 has demonstrated greater safety in use than nonoxynol-9 spermicides, which have been shown to increase users' risk in contracting HIV and other sexually transmitted diseases; it is also highly stable, easy to store, and easy to apply.[9]

## Adverse Events/Toxicity

In Phase I clinical trials, PRO 2000 was safe and well tolerated. Side effects were generally mild and infrequent and included vulvovaginal ulceration, irritation, itching, burning, bleeding, and mild gastrointestinal effects. Pain on passing urine was also reported.[10]

In a Phase I trial of 63 sexually active HIV uninfected women and abstinent HIV infected women, no serious adverse events were reported. Seventy-three percent of participants experienced at least one adverse event, of which 82% were classified as mild.[11] In a second Phase I trial of 73 abstinent HIV uninfected women, three women developed cervical abrasion. In both trials, the 0.5% gel formulation was better tolerated than the 4% gel formulation.[12]

During a Phase I safety and acceptability study of penile application of PRO 2000, no serious adverse events or urethral inflammation were reported following a week of daily PRO 2000 application in 72 HIV uninfected and 25 HIV infected men. Seventeen percent of uninfected participants and 4% of infected participants reported at least one mild adverse event.[13]

In a Phase I safety and acceptability study of the 0.5% gel formulation in 42 HIV uninfected women in Pune, India of low and higher risk for HIV transmission, 24 (57%) of the participants experienced at least one adverse event judged possibly related to product use. Of these 24, 7 (17%) participants experienced a moderate adverse event and 17 (40%) experienced only mild adverse events. No serious adverse events were observed.[14]

## Clinical Trials

For information on clinical trials that involve PRO 2000, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: PRO 2000 AND HIV Infections.

# PRO 2000

## Dosing Information

Mode of Delivery: Intravaginal.[15]

Dosage Form: The investigational product is an aqueous gel formulation containing 2% or 4% naphthalene 2-sulfonate polymer, a synthetic carbomer gelling agent, a pH 4.5 buffer, and a combination of preservatives.[16] In addition, a 0.5% gel was previously tested in healthy, sexually inactive women in the United Kingdom and Belgium [17] and in HIV uninfected, sexually active women in India.[18]

Storage: Store at 15 C to 35 C (59 F to 86 F) and protect from light.[19]

## Chemistry

CAS Name: 2-Naphthalenesulfonic acid, sodium salt, polymer with formaldehyde[20]

CAS Number: 29321-75-3[21]

Molecular formula:
(C10-H8-O3-S.C-H2O.Na)x-[22]

Molecular weight: Approximately 5 kD[23]

Physical Description: Light brown solid (active ingredient of PRO 2000).[24]

PRO 2000 is odorless and virtually colorless.[25]

Stability: Manufacturer data indicate that PRO 2000 is stable at 40 C and 75% relative humidity for 12 months.[26]

Solubility: Highly water-soluble (approximately 1 g/5 ml).[27]

## Other Names

Naphthalene 2-sulfonate polymer[28]

Formaldehyde-sodium 2-naphthalenesulfonate polymer[29]

PRO 2000/5[30]

PRO-2000[31]

## Further Reading


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# PRO 2000

## Manufacturer Information

PRO 2000
Indevus Pharmaceuticals, Inc.
99 Hayden Avenue, Suite 200
Lexington, MA 02421

## For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

## References


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2. Indevus Pharmaceuticals, Inc. - PRO 2000. Available at: http://www.indevus.com. Accessed 06/07/06.

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6. Protocol ID: HIVNET 020 - p. 1

7. Protocol ID: HIVNET 020 - pp. 3-4

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